REMARKS

Reconsideration is requested.

Claims 9-11 have been canceled, without prejudice. Claim 1 has been revised, without prejudice. Support for the revision may be found, for example, on page 7, lines 28-29 of the specification. No new matter has been added.

Claims 1-8 and 12 are pending. Claims 5-8 and 12 have been withdrawn from consideration.

The Section 112, second paragraph, rejection of claims 9-11 is moot in view of the above.

The Section 101 rejection of claims 9-11 is moot in view of the above.

To the extent not obviated by the above amendments, the Section 112, first paragraph "written description", rejection of claims 1 and 2 and the Section 112, first paragraph "enablement", rejection of claims 1-4, are traversed. Reconsideration and withdrawal of the rejections are requested in view of the above and the following further comments, as well as the attached.

The claims are submitted to be supported by an adequate written description. The applicants believe that one of ordinary skill in the art will appreciate that the applicants were in possession of the claimed invention at the time the application was filed. The claims are further submitted to be supported by an enabling disclosure. The applicants submit that one of ordinary skill in the art will be able to make and use the claimed invention without undue experimentation.

The applicants submit that the recitation of HDAC inhibitor in the claims is adequately supported by the specification. While the claimed invention has been exemplified in the specification with a particularly preferred compound, PXD101, the application as filed provides exemplification of the four broad chemical classes of HDAC inhibitor, i.e. Benzamide: MS-275; Hydroxamic acid: SAHA, PDX101, TSA; Small chain fatty acid: buyrate; and Depsipeptide: FR901228.

These compounds are described, for example, on pages 12-13 of the application. The fact that all of these compounds act as HDAC inhibitors was known at the time of filing of the present application and there is no reason to doubt that the use of any of these compounds with a PRAME inhibitor would provide the same results in terms of tumour treatment as did the exemplified pairing of RNAi and PDX101.

Attached for the Examiner's consideration, and listed on the attached PTO 1449 Form, is a copy of Epping et al., PNAS 104(45):17777-17782 (2007) together with the supplementary figures, which shows that members of all four of the above classes of HDAC inhibitor act in the same way with respect to PRAME.

Accordingly, (1) the activity of a benzamide HDACi (MS275) is shown in Figs 2e and 3c of Epping et al; (2) the activity of a hydroxamic acid (PDX101) is shown in Fig 2d of Epping et al and Fig 1d of the application as filed; (3) the activity of a hyrdoxamic acid (SAHA) is shown in Fig 3c of Epping et al; (4) the activity of a hydroxamic acid (TSA) is shown in SI Fig 9a of Epping et al; (5) the activity of a small chain fatty acid (butyrate) is shown in Fig 3c, SI Fig 9b of Epping et al; and (6) the activity of a

depsipeptide (spiruchostatin) is shown in Fig 2f and 3c and SI Fig 9 legend of Epping et al.

At the time the application was filed, one of ordinary skill in the art would have had no reason to have doubted that the results demonstrated for the particular PRAME inhibitor and HDACi could be extended to other known HDAC inhibitors. The later publication submitted herewith demonstrates that this is the case.

As can be seen from the present application at page 29 onwards, the present inventors discovered that PRAME suppresses the effects of the HDACi on cell proliferation. Prior to the present application, HDACi were known for use in the treatment of cancer and the present inventors discovered that PRAME expression confers cellular resistance to retinoic acid in human melanoma (page 35 of the application as filed) thereby reducing the beneficial effects of treatment of cancer with an HDACi. By inhibiting PRAME expression, treatment with an HDACi is more effective.

Given that the person of ordinary skill in the art at the time of the invention would know that HDAC inhibitors can be used in the treatment of cancer, there can be no doubt that that activity in any HDACi could be enhanced by the inhibition of PRAME.

The claims are adequately described in the present specification and one of ordinary skill in the art will be able to make and use the claimed invention without undue experimentation. Withdrawal of the Section 112, first paragraph, rejections is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned, preferably by telephone, in the event anything further is required.

Respectfully submitted,

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